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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/629,261	07/28/2003	Zheng Xin Dong	00537-186003	6695

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EXAMINER
LUKTON, DAVID

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 08/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/629,261	DONG, ZHENG XIN	
	Examiner	Art Unit	
	David Lukton	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16 and 19* is/are pending in the application.

4a) Of the above claim(s) *2,5-8 and 12-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,9-11,15,16 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Pursuant to the directives of the response filed 5/18/06, claims 1, 9, 15, 16 have been amended. Claims 1-16 & 19 remain pending Claims 6, 12-14 are withdrawn pursuant to the restriction. Claims 2, 5, 7, 8 are withdrawn because they do not encompass the elected specie. Claims 1, 3, 4, 9-11, 15, 16, 19 are examined in this Office action.

Applicants' arguments filed 5/18/06 have been considered and found persuasive in part. The "ODP" rejection of claim 1 over USP 6,903,186 is withdrawn, as is the provisional "ODP" rejection over S.N. 11/145782. In addition, the §103 rejection over Kjeldsen (USP 6,214,547) is withdrawn, at least for purposes of this Office action.

✧

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 4, 9-11, 15, 16, 19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

On pages 14-15, a procedure is given for assessing the propensity of a compound to displace (^{125}I) GLP-1(7-36) from RIN 5F rat insulinoma cells expressing the GLP-1 receptor. However, no result was given for this assay, and so there is no basis for concluding that any of the claimed peptides exhibits any capacity to bind to the GLP-1 receptor. It may well be the case that other analogs of GLP-1 bind to the GLP-1 receptor, but structure/activity relationships are unpredictable; i.e., one cannot predict GLP receptor binding merely by viewing the structure of a compound. Accordingly, "undue experimentation" would be required to use the compound of claim 10 to displace (^{125}I) GLP-1(7-36) from RIN 5F rat insulinoma cells expressing the GLP-1 receptor.

In response to the foregoing, applicants have begun by arguing that since the peptide of sequence ID NO:2 is no longer claimed, the examiner should not assert that a claim drawn solely to SEQ ID NO:2, were it to be presented, should be rejected. This particular point is actually correct; an examiner should not reject subject matter which is not claimed. This rejection, however, is directed at subject matter which <u>is</u> claimed, rather than subject matter which is not claimed. Applicants have also requested clarification as to which embodiments lack enablement. In response, fully 100% of all claimed embodiments lack enablement.

Applicants have also argued that the specification teaches how to make the claimed peptides. However, the examiner has never argued that "undue experimentation" would be required to synthesize any one of the claimed peptides. Next, applicants have argued that the specification discloses a method for determining whether or not the claimed peptides can bind to the GLP-1 receptor. Applicants have queried the examiner as to why it would require "undue experimentation" to test one peptide according to the assay. In response, the examiner would agree that to synthesize one peptide and to test that one peptide (according to the disclosed assay) would not require "undue experimentation". Further, to synthesize ten peptides, and to test each of them would probably also not require undue experimentation. But to synthesize, e.g., 1 million peptides, and to test each of them would require undue experimentation; even if a chemist (or group of chemists) were to undertake such a massive effort, the fact is that even then the skilled artisan would not be able to reliably "predict" that even one of those million peptides would bind to the GLP-1 receptor.

Proposing an assay (either *in vitro* or *in vivo*) will not convert an inactive compound into an active one. The reality in pharmacology is that minor changes in structure often eliminate activity. One cannot "predict" pharmacological efficacy merely by viewing the structure of a compound; the reality of this is not changed merely by the suggestion of an assay method.

The rejection is maintained.

✧

Claim 11 is rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 recites the phrase "effective amount", thereby rendering the claim indefinite as to the objective(s) of the amount.

✧

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this action.

A person shall be entitled to a patent unless -

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2 & 11 are rejected under 35 U.S.C. §102 (b) as being anticipated by Buckley (USP 5,545,618).

Buckley provides (col 2, line 56+) the sequence of native GLP-1(7-37), which is the following:

HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

Buckley also discloses GLP-1(7-34) and GLP-1(7-35). Claim 1, however, does not clearly exclude these. For example, in the case of GLP-1(7-35), there is one amino acid difference between this and the native GLP-1(7-36). That amino acid would be the arginine at position 36. Thus, one could say that there is one amino acid difference between GLP-1(7-35) and GLP-1(7-36)

In response, applicants have argued that if one begins with the 33 amino acid sequence $A^7 \ldots A^{39}$ (in which all amino acids are present) and proceeds to delete four of those amino acids, the result is a peptide in which the C-terminal amino acid is assigned position number 36, and the N-terminal amino acid, position number 7. However, this is not true. The C-terminal amino acid would be assigned position number 35, i.e., there would be 29 amino acids present.

The rejection is maintained.

✧

The following is a quotation of 35 USC. §103 which forms the basis for all obviousness rejections set forth in the Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where

the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 1-2 & 11 are rejected under 35 U.S.C. §103 as being unpatentable over Buckley (USP 5,545,618).

As indicated previously, Buckley provides (col 2, line 56+) the sequence of native GLP-1(7-37), which is the following:

HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

This particular peptide is excluded by the claims. However, as indicated previously, "obvious variants" are not.

In response, applicants have attempted to dismiss *In re Shetty* (**195** USPQ 753) and *In re Hass & Susie* (**60** USPQ 544) by arguing that when molecules are small and simple, these Court opinions apply, but when the compounds are "very large complex [and] biologically active", these decisions do not apply. Where applicants may have gotten such a notion is not explained. In fact, one could make the opposite argument, which is that the larger and more complex a compound is, the less that any one functional group contributes to its physical or biochemical properties (as a general proposition), and that therefor small structural

changes are better tolerated. Furthermore, the compounds at issue (in the claims) are not particularly "large" or "complex", as compared to, e.g., a protein or a polymer.

Next applicants have attributed to the examiner the following two assertions:

> a) if a given reference discloses the structure of one peptide, that reference necessarily discloses all possible homologous amino acid substitutions;
>
> b) the artisan of ordinary would be motivated to "select" all of the peptides disclosed in the reference.

As it happens, the examiner has not asserted either of the foregoing. Further, the first of these is clearly false. If a reference discloses one peptide, then it is a mere tautology to observe that the reference has disclosed just one peptide. According to applicants, however, if a reference discloses just one peptide, the skilled artisan would conclude that the reference has disclosed many peptides.

The examiner does not necessarily argue that if a reference discloses a given peptide, all "obvious variants" are immediately obvious to the artisan of ordinary skill. (Nor, however, does the examiner argue that they are not). For a given peptide of e.g., 30 amino acids, there might be 20 obvious variants; there might be 40. But one need not even attempt to place a number on it. What matters, with respect to the claimed invention, is that there exists <u>just one</u> that is obvious. The peptide biochemist of ordinary skill, upon reviewing the Buckley peptides, would have no difficulty recognizing at least one "obvious variant". Upon recognizing this, the requirements of the claims are met.

Applicants have also attempted to imply that the CAFC has overruled the *In re Shetty* (**195** USPQ 753) and *In re Hass & Susie* (**60** USPQ 544) cases. However, applicants have been unable to cite an opinion which has done this. Futher, it is evident that, at the time of *In re Dillon* (16 USPQ2d 1897), *Shetty* and *Hass* were still valid.

The rejection is maintained.

✧

Claim 1 and 11 are rejected under 35 U.S.C. §103 as being unpatentable over Knudsen (WO 98/08871).

Knudsen discloses various GLP-1 analogs, for example, those listed on pages 19-30. Applicants have attempted to exclude many of these, but without success.

In response, applicants have argued that each of the compounds disclosed by Knudsen contains a carboxynonadecanoyl group or a deoxycholic group. However, applicants are not correct.

In addition, as indicated previously, the exclusions, to the extent that they exist, only apply for the case of "E" representing OH or NH_2. The exclusions do not apply for the case of "E", taken together with the carbonyl group to which it is bonded, representing a carboxylate salt.

The rejection is maintained.

✧

Reference "EB" was stricken from the IDS because neither the complete document, nor a translation thereof has been provided.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached at (571)272-0562. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

D. Lukton

DAVID LUKTON, PH.D.
PRIMARY EXAMINER